Package leaflet: Information for the user

Givlaari 189 mg/mL solution for injection
givosiran

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Givlaari is and what it is used for

What Givlaari is
Givlaari contains the active substance ‘givosiran’.

What Givlaari is used for
Givlaari is used to treat acute hepatic porphyria in adults and adolescents aged 12 years and older.

What acute hepatic porphyria is
Acute hepatic porphyria is a rare illness that runs in families. It is caused by a defect in one of the proteins that make a molecule called haem in the liver. Because there is a problem in one of the proteins required to make haem, there is a build-up of some of the substances that are used to produce haem, namely aminolevulinic acid (ALA) and porphobilinogen (PBG). Having too much ALA and PBG can injure nerves and cause serious attacks of pain, nausea, muscle weakness and changes in mental functioning. Some people with acute hepatic porphyria may also have symptoms, such as pain and nausea, in between attacks. Longer-term complications that can be seen in people with acute hepatic porphyria include high blood pressure, chronic kidney disease and liver disease.

How Givlaari works
This medicine works by lowering the amount of an enzyme, called ALAS1, that controls how much ALA and PBG are made by the liver. By lowering ALAS1, the liver makes less ALA and PBG. This can help to reduce the effects of this illness.

2. What you need to know before you are given Givlaari

You must not be given Givlaari:
- if you have ever had a severe allergic reaction to givosiran or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor or nurse before you are given this medicine.

Severe allergic reaction
- Tell your doctor or nurse straight away if you get any signs of a severe allergic reaction. The signs are listed in "Serious side effects" in section 4.
- If you have a severe allergic reaction, your doctor or nurse will stop using the medicine straight away and you may need to take other medicines to control the symptoms.

Liver problems
Using this medicine can affect your liver. You will have blood tests to check your liver function before you start treatment with Givlaari and periodically during treatment. If these tests show abnormal results, your doctor or nurse will decide whether to interrupt treatment or stop treatment permanently. Abnormal results have been seen in some patients treated with this medicine, mainly between 3 to 5 months after starting treatment.

Kidney problems
Using this medicine can affect your kidneys, especially if you have already been diagnosed with kidney problems. Your doctor will check how your kidneys are working while you are using this medicine, especially if you already have kidney problems.

Children
This medicine should not be used in children below 12 years of age because there is no experience of using the medicine in this age group.

Other medicines and Givlaari
Tell your doctor or pharmacist if you are using, have recently used or might be using any other medicines.

When using certain medicines, this medicine may prolong or increase their effect or change their side effects.

Pregnancy
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or nurse for advice before using this medicine.

Breast-feeding
Studies in animals suggest this medicine may pass into breast milk. If you are breast-feeding ask your doctor for advice before taking this medicine. Your doctor will then help you decide whether to stop breast-feeding or to stop treatment with Givlaari taking into account the benefit of breast-feeding for your child and benefit of therapy for you.

Driving and using machines
This medicine is unlikely to have any effect on your ability to drive or use machines.

Givlaari contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per mL, that is to say essentially 'sodium-free'.

3. How Givlaari is given

How much Givlaari is given
Your doctor will work out how much medicine to give you. The amount will depend on your body weight.
- The recommended dose is 2.5 milligrams for every kilogram you weigh
- You will be given the medicine once a month (every 4 weeks)
- If blood tests show problems with your liver, your doctor may interrupt Givlaari treatment or stop treatment permanently. Your doctor may consider starting again at a lower dose.

How Givlaari is given
This medicine will be given to you once every month by a doctor or nurse. It is given as an injection under the skin (subcutaneously) into your stomach area (abdomen), or in some cases, your upper arm or thigh. The site of the injection will be rotated. If the dose is more than 1 mL, more than one vial will need to be used and more than one subcutaneous injection may need to be given.

If you are given too much Givlaari
In the unlikely event that your doctor or nurse gives you too much (an overdose) they will check you for side effects.

If you miss your dose of Givlaari
If you have missed an appointment for your injection, talk to your doctor or nurse as soon as possible. If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects
Severe allergic reactions (uncommon: may affect up to 1 in 100 people)
Tell your doctor or nurse straight away if you get any of the following signs of a severe allergic reaction (anaphylactic reaction) – the injection will need to be stopped and you may need to take other medicines to manage the reaction:
- swelling – mainly of the lips, tongue or throat which makes it difficult to swallow or breathe
- breathing problems or wheezing
- feeling dizzy or fainting
- rash, hives
- itching

Other side effects
Tell your doctor or nurse if you notice any of the following side effects:

Very common: may affect more than 1 in 10 people
- Nausea
- Redness, pain, itching or swelling at the site of the injection (injection site reaction)
- Skin rashes including red, itchy or dry skin, eczema or hives
- Feeling tired
- Blood tests showing an increase in transaminases, which are liver enzymes (a sign of possible liver inflammation)
- Blood tests showing an increase in creatinine, a substance removed from your body by your kidneys, or decrease in glomerular filtration rate (signs of possible kidney problems)

Common: may affect up to 1 in 10 people
- A type of allergic reaction (hypersensitivity) – with symptoms such as hives, rash, swelling of eyes, mouth or face, difficulty breathing, itching.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Givlaari

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and vial after EXP. The expiry date refers to the last day of that month.

This medicine is for single use only. Once the product is opened, use immediately.

Do not store above 25 °C.

Keep vial in the outer carton to protect from light.

Do not throw away any medicines via wastewater or household waste. Your doctor or nurse will throw away any medicines that are no longer being used. These measures will help protect the environment.

6. Contents of the pack and other information

What Givlaari contains
- The active substance is givosiran.
- Each mL contains givosiran sodium equivalent to 189 mg givosiran.
- The other ingredients are sodium hydroxide, phosphoric acid and water for injections.

What Givlaari looks like and contents of the pack
This medicine is a clear, colourless to yellow solution for injection.

Each pack contains one vial of 1 mL solution for injection.

Marketing Authorisation Holder and Manufacturer
Alnylam Netherlands B.V.
Antonio Vivaldistraat 150
1083 HP Amsterdam
Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
Alnylam UK Ltd.
Tel: 0800 141 2569 (+44 1628 878 592)
medinfo@alnylam.com

This leaflet was last revised in 01/2021

<--->

The following information is intended for healthcare professionals only:

Instructions for use

For subcutaneous use only.

- Collect materials not included in the pack that are needed for administration which will include a sterile syringe (1 mL or 3 mL), 21-gauge (G) or a larger needle, 25 G or 27 G needle and a sharps container.
- Calculate the required volume of Givlaari based on the recommended weight-based dose. If the dose is more than 1 mL, more than one vial will need to be used and more than one subcutaneous injection may need to be given. The maximum acceptable single injection volume to be administered is 1.5 mL.
- To withdraw Givlaari, hold the vial upright or tilt at a slight angle and ensure the flat edge of the needle is pointed downwards.
- Draw up the indicated injection volume with the 21 G or larger needle.
- Divide doses requiring volumes greater than 1.5 mL equally into multiple syringes, with each injection containing approximately the same volume.
- Point the needle and syringe straight up and tap the syringe to move any bubbles to the top. Once the bubbles are at the top, gently push the plunger to force the bubbles out of the syringe. Check to make sure you still have the correct amount of medicine in the syringe.
- Once the dose is prepared and in the administration syringe, replace the 21 G or larger needle with either a 25 G or 27 G needle.
- Note: Do not push this medicine into the 25 G or 27 G needle.
- Injection can be into the abdomen, or if required, the back or side of the upper arms, or the thighs. Consider rotating injection sites. Do not administer into scar tissue or areas that are reddened, inflamed, or swollen.
- Note: When administering subcutaneous injections into the abdomen, a 5.0 cm diameter circle around the navel should be avoided.
- Clean the area you intend to inject with an alcohol swab and wait for the area to dry completely.
- Ensure proper injection technique. Do not inject into a vein or muscle.
- Pinch and elevate the skin at the selected injection site. Insert the needle at a right angle (90 degrees) to deliver the injection just below the skin. In patients with little subcutaneous tissue or if the needle size is longer than 2.5 cm, the needle should be inserted at a 45-degree angle.
- Do not press down on the plunger while piercing the skin. Once the needle is inserted through the skin, release the pinched skin and administer the dose in a slow and steady manner. Once this medicine has been administered count for at least 5 seconds before withdrawing the needle from the skin. Lightly press gauze or cotton ball on the injection site as needed. Do not put the needle cap back on.
- Note: Don’t aspirate after inserting the needle to prevent tissue damage, haematoma and bruising.
- If more than one injection is needed for a single dose of Givlaari, the injection sites should be at least 2 cm apart from previous injection locations.
- Only use the vial once. After you inject the dose, dispose of any unused medicine in the vial according to local regulations.
- Use the syringes, transfer needles and injection needles only once. Dispose of any used syringes and needles in accordance with local requirements.